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10/083,466	02/27/2002	Yasuhisa Sakurai	2002-0303	5812

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EXAMINER	
CELSA, BENNETT M	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 03/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/083,466	SAKURAI ET AL.	
	Examiner	Art Unit	
	Bennett Celsa	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/27/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1-8 are currently pending.

Election/Restriction

1. Applicant's election of DNA (e.g. salmon testes DNA as the macromolecular drug) and PEG-P(Lys) as the block copolymer in the correspondence dated 12/23/04 which reads on claims 1-8 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-8 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Harada et al., Macromolecules, Vol. 28 (Abstract: 6/95: article 7/95) pages 5294-5299.

The presently claimed invention is drawn to a macromolecular micelle drug composition, comprising:

a. a macromolecular drug (of opposite charge w/r to the drug carrier; e.g. protein/DNA etc.); and

b. a drug carrier comprising a block copolymer having a "non-charged segment" (e.g. PEO, PEG etc.) and a "charged segment" (e.g. polyamino acid; i.e. poly Lys; poly asp etc.). (e.g. see claim 1).

And a method of carrying a chargeable drug on a carrier comprising mixing the chargeable drug with the carrier on the carrier comprising mixing (e.g. see claim 7).

Elected embodiment:

"macromolecular drug" = DNA

"non-charged segment" =PEG

"charged segment "= poly-Lys

Harada et al. disclose, in the abstract and the article, a PEG-polylysine block copolymer (e.g. see page 5295 col. 1) and a PEG-polyaspartic acid block copolymer (e.g. see page 5295 col. 1) and a heterogenous mixture thereof to form polyion complex micelles. The disclosure of the block copolymer separately and in admixture anticipate present claims 1-5. The Abstract comments as to the potential use of the polyion complex micelles as vehicles for charged compounds (e.g. drug delivery of proteins and nucleic acids) and the article further discloses that

peptides have been already included within the core of the polyion complex micelles which is segregated from the outside aqueous layer (e.g. see page 5298). Accordingly, one of ordinary skill in the art would immediately envisage (e.g. anticipate) the incorporation of peptides/nucleic (of opposite charge) into the core charged layer of the polyion complex micelle (e.g. utilizing the charged environment of the core) for purposes of drug delivery. Alternatively, it would have been prima facie obvious to the skilled artisan to utilize the polyion complex micelle of this reference for drug delivery.

5. Claims 1-5 and 7 are rejected under 35 U.S.C. 102(b) as anticipated , or alternatively under 35 U.S.C. 103 as being obvious over Yokoyama et al., Crit. Rev. Ther. Drug Carrier Syst. (1992) Vol. 9/3-4 (pages 213-248).

The presently claimed invention is drawn to a macromolecular micelle drug composition, comprising:

a. a macromolecular drug (of opposite charge w/r to the drug carrier; e.g. protein/DNA etc.); and

b. a drug carrier comprising a block copolymer having a "non-charged segment" (e.g. PEO, PEG etc.) and a "charged segment" (e.g. polyamino acid; i.e. poly Lys; poly asp etc.). (e.g. see claim 1).

And a method of carrying a chargeable drug on a carrier comprising mixing the chargeable drug with the carrier on the carrier comprising mixing (e.g. see claim 7).

Elected embodiment:

"macromolecular drug" = DNA

"non-charged segment" =PEG

"charged segment "= poly-Lys

The Yokoyama et al. review article describes the strategy of employing block copolymers as drug carriers, especially A-B type block copolymers (e.g. see pages 214-215) which advantageously form polymeric micelles with their attendant benefits (e.g. high water solubility, high structural stability: see pages 228-230). Yokoyama discloses a composition of "polymeric micelles" which were "formed by noncovalent interchain interactions" comprising PEG-polyasp block copolymer and a drug (e.g. adriamycin which is clearly w/n the present claim scope as disclosed in the present specification) . PEG is a "non-charged segment" and Polyasp is a "charged segment" within the scope of the presently claimed invention. The formation of a micelle using a macromolecular drug composition within the scope of the presently claimed invention would render the drug "having an opposite charge carried electrostatically on said drug carrier" inherent in the reference composition. It is noted that the Examiner lacks the facilities necessary to make a comparison with the prior art composition.

6. Claims 1-8 are rejected under 35 U.S.C. 102(e) as anticipated by Torchilin et al. US Pat. No. 5,746,998 (5/98: filed 6/94).

The presently claimed invention is drawn to a macromolecular micelle drug composition, comprising:

a. a macromolecular drug (of opposite charge w/r to the drug carrier; e.g. protein/DNA etc.); and

b. a drug carrier comprising a block copolymer having a "non-charged segment" (e.g. PEO, PEG etc.) and a "charged segment" (e.g. polyamino acid; i.e. poly Lys; poly asp etc.). (e.g. see claim 1).

And a method of carrying a chargeable drug on a carrier comprising mixing the chargeable drug with the carrier on the carrier comprising mixing (e.g. see claim 7).

Elected embodiment:

"macromolecular drug" = DNA

"non-charged segment" =PEG

"charged segment "= poly-Lys

Torchilin et al. disclose and claim "macromolecular micelle compositions" comprising:

a hydrophilic polymer "linked" to a hydrophobic polymer and a "target ligand" "linked" to either the hydrophilic or hydrophobic polymers. "Linked" is defined to encompass BOTH covalent or *noncovalent* bonding (e.g. see col. 2, line 13-15). The "hydrophilic polymers" are "uncharged" (e.g. see col. 2, lines 18) and preferably include PEG (e.g. see col. 2, lines 15-27; examples and patent claim 4). The "hydrophobic polymers" of the reference include a "polymeric backbone" which incorporates "charged" polymers within the scope of the presently claimed invention (e.g. see col. 2, lines 33-37) preferably poly-L-lysine (e.g. see patent claim 6). It is noted that patent claim 14 is specifically directed to PEG-polylysine. Targeting ligands (e.g. carried) include drugs within the scope of the presently claimed invention including "proteins" such as antibodies, hormones, enzymes, sugars (e.g. polysacharides) (see e.g. bottom of col. 9-

10; patent claims 21-23). The reference teaching of PEG-polysine which is non-covalently linked to a targeting ligand which is a drug which includes a markush of proteins/peptides/sugars all of which are macromolecules within the scope of the presently claimed invention would anticipate the presently claimed invention. Since the drugs and drug carriers within the scope of the presently claimed invention are mixed to effect entrapped drugs by formation of micelles the mechanism (e.g. opposite charges of carrier and macromolecule) of such micelle formation would be inherent.

7. Claims 1-5 and 7 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Yokoyama et al., U.S. Pat. No. 5,449,513 (9/95: filed 8/93).

The presently claimed invention is drawn to a macromolecular micelle drug composition, comprising:

a. a macromolecular drug (of opposite charge w/r to the drug carrier; e.g. protein/DNA etc.); and

b. a drug carrier comprising a block copolymer having a "non-charged segment" (e.g. PEO, PEG etc.) and a "charged segment" (e.g. polyamino acid; i.e. poly Lys; poly asp etc.). (e.g. see claim 1).

And a method of carrying a chargeable drug on a carrier comprising mixing the chargeable drug with the carrier on the carrier comprising mixing (e.g. see claim 7).

Elected embodiment:

"macromolecular drug" = DNA

"non-charged segment" =PEG

"charged segment "= poly-Lys

Yokoyama discloses drug carriers composed of a block copolymer having hydrophilic and hydrophobic segments; a polymeric micelle drug comprising hydrophobic drugs trapped by physical treatments in said drug carrier and methods for trapping hydrophobic drugs in the drug carrier (e.g. see Abstract and columns 1-2). The patent compound generics (e.g. col. 1 and columns 3-4) anticipate, or in the alternative render obvious, compound species of the presently claimed invention e.g. see present claim 4, when X is 0 for the structures I and II. The disclosed preferred species (e.g. col. 2, formula 3: Polyethyleneoxide-poly benzyl asp and incorporated drugs in examples 1-7 anticipate the presently claimed invention. See also patent claims.The Yokoyama drugs include macromolecules such as adriamycin (e.g. see examples and patent claims) which is clearly w/n the scope of the presently claimed invention (e.g. its disclosed in the present specification). Since the drugs and drug carriers within the scope of the presently claimed invention are mixed to effect entrapped drugs by formation of micelles the mechanism (e.g. opposite charges of carrier and macromolecule) of such micelle formation would be inherent.

8. Claims 1-8 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kabanov et al. US Pat. No. 5,656,611 (8/97: filed 11/94).

The presently claimed invention is drawn to a macromolecular micelle drug composition, comprising:

a. a macromolecular drug (of opposite charge w/r to the drug carrier; e.g. protein/DNA etc.); and

b. a drug carrier comprising a block copolymer having a "non-charged segment" (e.g. PEO, PEG etc.) and a "charged segment" (e.g. polyamino acid; i.e. poly Lys; poly asp etc.). (e.g. see claim 1).

And a method of carrying a chargeable drug on a carrier comprising mixing the chargeable drug with the carrier on the carrier comprising mixing (e.g. see claim 7).

Elected embodiment:

"macromolecular drug" = DNA

"non-charged segment" =PEG

"charged segment "= poly-Lys

Kabanov et al. disclose compositions comprising polynucleic acid polymers (e.g. RNA/DNA) associated (e.g. complexed) upon mixing with block copolymers of alkylethers and a polycationic polymer with the composition further optionally comprising "targeting adducts" (e.g. antibody, hormones, drugs). Eg. See abstract; col 1, lines 1-12; col. 12, lines 35-55. The reference teaching of "polyether/polycation" polymers (e.g see structure II and VI-a in col. 3) in which the polyether is the uncharged segment while the polycation is the charged segment which associates with the DNA upon mixing would anticipate the presently claimed generic embodiment. Additionally, the block copolymer formed by use of the reference preferred polycation: polylysine (e.g. see col. 10: structures XVIII-XX; col. 6, lines 60-65; example 11); and the reference preferred polyether: PEG compound (e.g. see col. 20-21 and examples 13-

15), would anticipate, or in the alternative, render obvious the selection of PEG-P(Lys) as the block copolymer which is associated with polynucleic acid polymers (e.g. RNA/DNA) alone or with the disclosed "targeting adducts" (e.g. drugs, antibodies, hormones). Since the drugs and drug carriers within the scope of the presently claimed invention are mixed to effect entrapped drugs by formation of micelles the mechanism (e.g. opposite charges of carrier and macromolecule) of such micelle formation would be inherent.

Relevant Prior Art Documents:

1. Ballou et al. US Pat. No. 5,198,360 (3/93): col.31, lines 1-5 teach the public availability (e.g. purchased from Sigma Chemical Co.) of salmon testes DNA.

Future Correspondences

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bennett Celsa whose telephone number is 571-272-0807. The examiner can normally be reached on 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bennett Celsa
Primary Examiner
Art Unit 1639

BC
March 8, 2005